REMARKS

Following entry of the present amendment, claims 32-37 and 40-73 will be pending, new claims 69-73 having been added. Support for amended claim 35 and the new claims can be found throughout the specification. In particular, support for the amendment of claim 35 can be found at page 10, lines 12-14. Support for new claims 69-73 can be found at page 4, lines 7-10, page 5, lines 17-19, page 10, lines 12 and 26-27, and page 21, lines 8-10. No new matter has been introduced.

Applicant thanks the Examiner for acknowledging on page 1 of the Action that claims 32-34, 40-42, 44-46 and 48 are allowable. It is believed that the statement to the contrary at the bottom of page 9 of the Action was made in error.

I. REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ENABLEMENT

The Examiner rejected claims 49-68 for failing to provide enablement for an isolated nucleic acid that encodes SEQ ID NOs:1 or 10 with 1-50 conservative amino acid substitutions. See the Action, item 6 at page 3. After considering the Wands factors for determining enablement/non-enablement, see In re Wands, 858 F.2d 731 (Fed. Cir., 1988), the Examiner alleged that *undue experimentation* was necessary to practice the claimed invention by a person with ordinary skill in the pertinent art. In particular, it was the Examiner's position that, in the instant case, (1) the amount of experimentation was immense, (2) the specification provided no guidance or directions, (3) the specification was devoid of any working examples, (4) the nature of the invention was DNA encoding a transcriptional regulatory factors comprising bromodomains, (5) the prior art showed other transcriptional factors containing bromodomains, (6) the relative level of skill in this art was very high, (7) the predictability of the art was low, and (8) the claims were broad. See the Action, item 6 at pages 4-5.

Applicant disagrees with the Examiner's analysis based on the Wands factors when applied in the instant application for the reasons set forth below:

(1) The breadth of the claims

First, the Examiner has seriously misconstrued the breath of most of the rejected claims, apparently believing they all recite nucleic acids that encode SEQ ID NOs:1 or 10 with 0-50 conservative amino acid substitutions. That description applies only to claims 49, 60, 63 and 66. The rest of the rejected claims span a variety of different scopes, some much narrower than claim 49, others broader. Nowhere does the rejection address the limitations in these other claims. For the Examiner's benefit, the claims are described below.

Claim 49 is drawn to an isolated nucleic acid encoding polypeptide having the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:10 with 0-50 conservative amino acid substitutions. The polypeptide can bind to hSNF2H, hSNF2L or NCoA-62/Skip. Claims 60 and 63 are respectively drawn to a vector and a cultured host cell, each comprising the nucleic acid of claim 49. Claim 66 is directed to a method of producing a polypeptide encoded by the nucleic acid of claim 49. Claims 50, 51 and 58 depend from claim 49, limiting the maximum number of conservative substitutions to 30, 10 and 3, respectively.

Claims 52-54 cover nucleic acids having nucleotide sequences that are respectively at least 70%, at least 90%, or at least 95% identical to SEQ ID NO:2 or SEQ ID NO:9. These nucleic acids encode polypeptides containing at least one bromodomain and binding to hSNF2H, hSNF2L or NCoA-62/Skip. Claims 61 and 64 are respectively directed to a vector and a cultured host cell, each comprising the nucleic acid of claim 52. Claim 67 is directed to a method of producing a polypeptide encoded by the nucleic acid of claim 52.

Claims 55-57 cover nucleic acids encoding polypeptides the respective amino acid sequences of which are at least 60%, at least 80%, or at least 95% identical to SEQ ID NO:1 or SEQ ID NO:10. Again, these polypeptides bind to hSNF2H, hSNF2L or NCoA-62/Skip. Claims 62 and 65 are respectively directed to a vector and a cultured host cell, comprising the nucleic acid of claim 55. Claim 68 covers a method of producing a polypeptide encoded by the nucleic acid of claim 55.

Second, Applicant does not understand why the Examiner has concluded that the rejected claims "read on any nucleic acids that encode proteins similar to SEQ ID NOs:1 or 10 having the

original function, some altered function or no function at all." See the Action, item 6, second paragraph, at page 3. It appears that the Examiner has overlooked the limitation, present in each of the rejected claims, requiring that the encoded polypeptide "binds to a protein selected from the group consisting of hSNF2H, hSNF2L, and NCoA-62/Skip." Thus, none of the rejected claims can read on a nucleic acid that encodes a protein having "no function at all."

Accordingly, the breadth of each of the rejected claims is not at all as the Examiner has characterized it.

(2) The amount of direction or guidance presented

Applicant disagrees with the Examiner's position that the specification provides no guidance "since there is no discussion of where in the protein the activity is localized and no information is provided as to where one could make modifications and still maintain the function." See the Action, pages 4-5. To the contrary, the instant specification discloses a number of functional domains of SEQ ID NO:1 (TCoA1), i.e., two C4HC3 zinc-fingers at amino acid positions 254-295, one bromodomain at amino acid positions 2684-2747, and one extensive glutamine-rich region at amino acid positions 1840-2400. See Figure 1 and Example 4 at pages 27-28. Further, Example 6 teaches that a fragment of TCoA1 representing residues 85-247 is involved in binding to hSNF2H, hSNF2L, and NCoA-62/Skip. See pages 29-30. One of ordinary skill would have found a great deal of guidance in the specification regarding what portions of the sequence should not be changed or should have only conservative changes, in order to preserve function. In addition, the specification also identifies groups of amino acids having conserved side chains and teaches how to make conservative amino acid substitutions, i.e., replacing one amino acid with another from the same group. See page 8, lines 22-30, and page 9, lines 1-2.

With the benefit of the above information, a person having ordinary skill in the pertinent art would know how to make functional equivalents of TCoA1. Accordingly, a skilled person in the art also would know how to make the claimed nucleic acids that encode these functional equivalents. In other words, the instant application provides sufficient guidance and directions for how to practice claims 49-68.

(3) The quantity of experimentation necessary

Applicant agrees that the quantity of experimentation for practicing the full scope of some of the broader claims is large. This fact, however, does not compel the conclusion that the specification fails to enable claims 49-68. As the Examiner pointed out, "[c]learly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention." See the Action, page 4, second paragraph. A considerable amount of experimentation is permissible when the experimentation needed is merely routine, or when the specification in question provides a reasonable amount of guidance of how the experimentation should be performed. See In re Wands, at 737.

In the pertinent field of molecular biology, it is routine experimentation to isolate or make nucleic acids homologous to a defined nucleotide sequence. In addition, the instant application, as discussed above, provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed, i.e., what type of amino acid substitutions to make and where to insert these substitutions in the protein so that the modified protein maintains the function. The specification also teaches methods of isolating transcriptional regulatory factors with function equivalent to TCoA1. See page 7, lines 24-30. Thus, the quantity of experimentation needed to make and use all embodiments of claims 49-68 does not render the experimentation undue pursuant to Wands.

(4) The predictability of the art

The Examiner stated that the "predictability of the art is low since it is not possible to predict which changes will result in functional polypeptides." See the Action, page 5, first paragraph. Applicant disagrees. First, the variations in claims 49-51, 58, 60, 63 and 66 are limited to "conservative amino acid substitutions," which, as generally known in the art, will tend not to have substantial effects on protein function. Second, claims 49-68 also recite a functional limitation, i.e., binding to a protein selected from the group consisting of hSNF2H, hSNF2L, and NCoA-62/Skip. As mentioned above, the region defined by residues 85-247 of TCoA1 is involved in the interaction with hSNF2H, hSNF2L, and NCoA-62/Skip. Accordingly, those skilled in the art would readily recognize that, to obtain the nucleic acids as claimed, they

should avoid inserting mutations in the region encoding the above functional domain, or make only conservative substitutions. Third, Applicant points out that SEQ ID NO:1 and SEQ ID NO:10 consist of 2901 and 2781 amino acids, respectively. Fifty amino acid substitutions would result in changes of only 1-2% amino acids of each protein. This is a relatively tiny degree of change overall. Taken together, it is highly predictable that TCoA1 mutants having up to 50 conservative amino acid substitutions outside the region of amino acids 85-247, will retain the binding activity to hSNF2H, hSNF2L, or NCoA-62/Skip.

It is even more predictable that making 30 or fewer changes (as set forth in claim 50) can be done without affecting function of the polypeptide. The Examiner has not explained why he believes claim 50 to be invalid for lack of enablement. Even less apparent is why the Examiner believes claim 51 (10 or fewer substitutions) and claim 58 (3 or fewer!) cannot be practiced by one of ordinary skill without undue experimentation.

The Examiner does not even address the limitations of claims 52-57, 59, 61, 62, 64, 65, 67, or 68, in the context of the enablement rejection, so it is difficult for Applicant to know how to respond to this part of the rejection. If it is based on the same sort of considerations as set forth in the Action regarding the enablement rejection of claim 49, then Applicant reiterates that in fact the claims do specify a function of the encoded polypeptide and the specification does provide a great deal of guidance as to the important regions of the polypeptide. Furthermore, each of claims 52-57, 59, 61, 62, 64, 65, 67 and 68 specifies that the polypeptide contain "at least one bromodomain," a structural limitation nowhere noted by the Examiner.

After weighing all factual considerations related to the enablement issue, Applicant submits that the instant application, when filed, contained sufficient information regarding the subject matter of claims 49-68 to enable one skilled in the pertinent art to make and use the nucleic acids, vectors, cells, and methods encompassed by these claims. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection of claims 49-68 for lack of enablement.

II. REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 49-68 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to a skilled person in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. It is the Examiner's position that the specification does not meet this standard of written description. See the Action, item 7 at pages 5-8. Applicant respectfully traverses each of the Examiner's grounds for this rejection below.

The Examiner alleged that the "only identifying characteristics of the claimed nucleic acids are the percent of identity to base sequences" and that the specification failed to disclose a "correlation between the function and the different sequences encoding the polypeptides that are less than 100% identical." See the Action, page 7, last paragraph.

With regard to this allegation, Applicant points again to the functional limitation in each of the independent claims: i.e., the encoded polypeptide "binds to a protein selected from the group consisting of hSNF2H, hSNF2L, and NCoA-62/Skip." Applicant also points to Example 6 of the specification at pages 29-30, which discloses that a region defined by residues 85-247 of SEQ ID NO:1 is involved in interacting with hSNF2H, hSNF2L, and NCoA-62/Skip. This region of SEQ ID NO:1 represents only 5.6% of the entire length of SEQ ID NO:1. It would be trivial to include more of SEQ ID NO:1 to bring this up to 60%, 80%, or 95%, as recited in claims 55, 56 and 57, respectively, while preserving the function localized in this region. Plainly one of ordinary skill would understand this.

The standard for determining compliance with the written description requirement is whether the description clearly informs persons of ordinary skill in the art that the inventor was in possession of the claimed invention as a whole at the time the application was filed. In the context of biotechnology inventions (such as the present invention), the written description requirement can be met by disclosing "sufficiently detailed, relevant identifying characteristics ... i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and

structure, or some combination of such characteristics." See Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 964 (Fed. Cir. 2002).

Claims 49-58 relate to nucleic acids that encode TCoA1, a bromodomain-containing transcriptional regulator, and certain related polypeptides that are capable of binding to hSNF2L, hSNF2H or NCoA-62/Skip. These claimed nucleic acids are described by their structural characteristics (e.g., comprising a nucleotide sequence that is least 70% homologous to SEQ ID NO:2 or SEQ ID NO:9, as in claim 52), and by functional and/or structural characteristics of the encoded polypeptide (e.g., containing at least one bromodomain; binds to a defined protein).

Moreover, the specification discloses not only the full amino acid sequences of TCoA1 (SEQ ID NO:1) and its variant (SEQ ID NO:10), but also a correlation between the function specified in all of the rejected claims and the structure that possesses the function, i.e., the region of SEQ ID NO:1 at residues 85-247 that is important for interacting with hSNF2H, hSNF2H and NCoA-62/Skip. Thus, one skilled in the art would be able to predict the whole structure of the polypeptide encoded by the claimed nucleic acids based on its structural similarity and functional equivalence to TCoA1. Since the genetic code is widely known, disclosure of an amino acid sequence would provide sufficient information such that an artisan in the pertinent art would recognize that the applicant was in possession of the full genus of nucleic acids encoding the amino acid sequence. *See* In re Bell, 991 F.2d 781.

Taken together, the instant specification describes the nucleic acids of claims 49-58 by a combination of identifying characteristics so sufficiently detailed and relevant that one skilled in the pertinent art would conclude that Applicant was in possession of the claimed invention at the time the application was filed. By the same token, the specification also provides sufficient written description for the subject matter covered by claims 59-68, which depend from claims 49, 52, and 55. Applicant thus submits that he has met the burden established by Section 112, first paragraph.

The Examiner further alleged that "[t]here is no disclosure of how any portion of the sequence gives rise to a polypeptide having the transcriptional regulatory function." See the Action, page 7.

Since none of the claims recites "transcriptional regulatory function" or anything comparable, the Examiner's concern is not understood. There is no need for the specification to disclose the portion of the sequence required for "transcriptional regulatory function." Nonetheless, Applicant points out that in fact the specification discloses the motifs found in TCoA1 that are common to bromodomain-containing transcriptional factors. See, for example, page 6, lines 13-30, of the specification. Given the correlation between structure and function of a protein, one skilled in the art would understand that these regions in TCoA1 must play important roles in "transcriptional regulatory function."

For the reasons set forth above, it is submitted that Applicant has successfully traversed the Examiner's grounds for rejection of claims 49-68 for lack of sufficient written description. Applicant, accordingly, requests withdrawal of this rejection.

The Examiner also rejected claims 35-37, 43 and 47 under Section 112 as failing to comply with the written description requirement. Specifically, the Examiner pointed out that while the specification defines 50°C as moderate stringency, claim 35 recites 50°C as high stringency conditions for hybridization. For the sole purpose of moving this application forward, Applicant has amended claim 35 to replace "high stringency conditions" with the term "stringent conditions," thereby rendering this rejection moot.

III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 35-37, 43 and 47 are rejected under Section 112, second paragraph, as being indefinite. In particular, the Examiner alleged that these claims were incomplete since there was no temperature defined for the wash step. See the Action, item 10 at page 9.

Amended claim 35 recites "the stringent conditions comprise hybridization and washing at 50°C in 2X SSC containing 0.1% SDS." The specification at page 10, lines 10-14, states:

> The stringency of hybridization is defined as equilibrium hybridization under the following conditions: 42°C, 2x SSC, 0.1% SDS (low stringency); 50°C, 2x SSC, 0.1% SDS (medium stringency); and 65°C, 2x SSC, 0.1% SDS (high stringency). If washings are necessary to achieve equilibrium, the washings are performed with the hybridization solution for the particular stringency desired.

A person with ordinary skill in the pertinent art will interpret this statement as implying that the wash steps are carried out under the same conditions, e.g., temperature and solution, as the hybridization step (i.e., "for the particular stringency desired"). Since amended claim 35 defines the temperature of the wash steps, it renders this indefiniteness rejection moot.

IV. OBJECTION TO THE SPECIFICATION

The Examiner objected to the specification as containing embedded hyperlinks. Following the Examiner's instruction, Applicant has deleted http:// at page 11, line 11, and page 26, line 10.

CONCLUSION

In summary, for the reasons set forth herein, Applicant maintains that claims 35-37, 43, 47, and 49-68 clearly and patentably define the invention. Applicant respectfully requests that the Examiner reconsider the rejections set forth in the Action.

The necessary additional claim fees in the amount of $650 are being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. A Petition for Extension of Time is also filed herewith.

Apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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